REMARKS/ARGUMENTS

By this Amendment, claims 2, 76-79, and 81 are canceled, claims 1, 3, 54, 69, 80, 82, and 85 are amended, and claim 88 is added. Claims 5, 6, 15, 17-25, 35-40, 46, 47, 53, 57-68, 74 and 87 have been withdrawn from consideration pursuant to a restriction requirement by the Examiner. Claim 84 is "constructively" canceled since it was inadvertently omitted from the original claim listing and never presented.

Claims 1, 3-4, 7-14, 16, 26-34, 41-45, 48-52, 54-56, 69-73, 75, 80, 82-83, 85-86, and 88 are pending.

Support for amending of claim 1 can be found in the original disclosure, e.g., on page 21, lines 13-17, 20-21 and on page 25, lines 1-2.

Claims 3, 69, 80, 82 and 85 are amended to reflect the proper dependency.

Claim 54 is amended to correct a typographic error.

Claim 69 is amended to correct the antecedent basis in the response to the Examiner's objection.

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Claim Rejections: 35 USC § 112

Rejections of claims 76-82 under 35 U.S.C. 112, second paragraph are moot due to cancellation of claims 76-79 and 81. Claims 80 and 82 as amended depend from claim 51 and are now in compliance with 35 U.S.C. 112, second paragraph.

Claim Rejections: 35 USC § 102

Lewis et al. (Bioconjugate Chem. 2002, 13: 1176-1180)

Claims 1-4, 28-32, 34, 69, 71-73, 76, 80, 81, 83, 85 and 86 stand rejected under 35 U.S.C. 102(b) as being anticipated by Lewis et al. (Bioconjugate Chem. 2002, 13: 1176-1180), as evidenced by Basu et al. (Bioconjugate Chem, 1997, 8: 481-488).

This rejection is respectfully traversed. Claim 1 as amended obviates the rejection under 35 U.S.C. 102(b). The rejection is moot with respect to claims 2, 76 and 81, which have been canceled.

To anticipate a claim, the reference must teach every element of the claim. MPEP §2131.

The Lewis et al. reference does not identically disclose each and every element recited in the claims because it does not disclose a conjugate comprising "a targeting moiety that is capable of binding to a cell surface molecule or being bound by a cell surface molecule" which is covalently linked to PNA.

On page 4 of the Office Action, the Examiner stated that

> Lewis et al. teach a DOTA-PNA conjugate designed to target *bcl-2* (i.e., an oncogene), wherein DOTA comprises a radiometal (i.e., a polymeric diagnostic moiety) and wherein the PNA, which is 18 bases long, is further coupled to a peptide designated for intracellular delivery of the radiolabeled PNA (i.e., a targeting moiety); the targeting peptide and DOTA are conjugated to PNA via linkers (Abstract, p. 1177, Fig. 1). Lewis et al. teach contacting cells known to comprise high and low levels of *bcl-2* with the DOTA-PNA-peptide conjugate, allowing for the conjugate to be internalized by the cells, and detecting the conjugate within the cells to determine the level of expression of *bcl-2* transcript (emphasis added).

The Examiner improperly equates a peptide designated for intracellular delivery of the

radiolabeled PNA (i.e., a membrane permeating peptide PTD-4) with a targeting moiety of the present invention which is defined in the specification on page 21, lines 20-21 as "a moiety that "comprises any chemical substance that is capable of binding to a cell surface molecule or being bound by a cell surface molecule (e.g., a receptor)." Targeting the conjugate of the invention to a cell surface receptor so that the internalization is achieved via a receptor provides the desired specificity. This specificity cannot be achieved when a membrane permeating peptide is used instead of a cell surface receptor. Therefore, the membrane permeating peptide as described in Lewis et al. does not constitute a "targeting moiety" contemplated in this invention. Consequently, the Lewis et al. reference does not anticipate the invention because it does not identically disclose each and every element recited in claim 1 (i.e., a targeting moiety).

Claims 3-4, 28-32, 34, 69, 71-73, 80, 83, 85, 86 and 88 depend from base claims 1 and are not anticipated by Lewis et al. for at least the same reasons claim 1 is not anticipated.

Accordingly, reconsideration and withdrawal of Sections 102(b) rejections of base claim 1 and dependent claims 3-4, 28-32, 34, 69, 71-73, 80, 83, 85, 86 and 88 are respectfully requested.

Tomalia et al. (U. S. Patent No. 5,714,166)

Claims 1, 2, 4, 7-10, 12-16, 26-28, 34, 41-45, 48, 49, 52, 54-56, 69, 70, 73, 75, 83, 85 and 86 are rejected under 35 U.S. C. 102(b) as being anticipated by Tomalia et al. (U. S. Patent No. 5,714,166), as evidenced by Basu et al.

This rejection is respectfully traversed. Claim 1 as amended obviates the rejection under 35 U.S.C. 102(b). The rejection is moot with respect to claim 2 which has been canceled.

The Tomalia et al reference does not identically disclose each and every element recited in the claims because it does not disclose a compound in which PNA is covalently linked to a targeting moiety (e.g., a cell receptor).

Tomalia et al. teach that a targeting director can be a PNA associated with a dendrimer (see col. 28, lines 9-27).

Also, Tomalia et al. teach that genetic material can be complexed with a dendrimer only via a non-covalent association (see col. 47, lines 55-62). Thus, Tomalia et al. do not teach a compound comprising a dendrimer (X) covalently linked to a PNA (P), which is, in turn, covalently linked to a targeting moiety. (T), wherein the compound is represented by a formula X-L1-P-L2-T or pharmaceutically acceptable salts thereof, wherein L1 and L2 represent at least one linking moiety.

Hence, the Tomalia et al. reference does not anticipate the invention because it does not identically disclose each and every element recited in claim 1 (i.e., covalent binding of PNA to a targeting moiety).

Claims 4, 7-10, 12-16, 26-28, 34, 41-45, 48, 49, 52, 54-56, 69, 70, 73, 75, 83, 85, 86 and 88 depend from base claims 1, and are not anticipated by Lewis et al. for at least the same reasons claim 1 is not anticipated.

Accordingly, reconsideration and withdrawal of Sections 102(b) rejections of base claim 1 and dependent claims 4, 7-10, 12-16, 26-28, 34, 41-45, 48, 49, 52, 54-56, 69, 70, 73, 75, 83, 85, 86 and 88 are respectfully requested.

Claim Rejections: 35 USC § 103

Tomalia et al. in view of Meade et al. (U.S. Patent 6,713,046)

Claims 1, 2, 4, 7-16, 26-28, 34, 41-45, 48, 49, 52, 54-56, 69, 70, 73, 75, 83, 85 and 86 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Tomalia et al., as applied to claims 1, 2, 4, 7-10, 12-16, 26-28, 34, 41-45, 48, 49, 52, 54-56, 69, 70, 73, 75, 83, 85, and 86 above, in view of Meade et al. (U.S. Patent 6,713,046).

This rejection is respectfully traversed. Claim 1 as amended obviates the rejection under 35 U.S.C. 103(a). The rejection is moot with respect to claim 2, which has been canceled.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion of motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or reference when combined) must teach or suggest all the claim limitations. MPEP § 2143. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Base claim 1 as amended obviates the rejection. Applicants take the position that there is no *prima facie* case of obviousness for the present claims over cited US patents taken alone or in combination. None of the above references teach or suggest a compound comprising a dendrimer (X) covalently linked to a PNA (P), which is, in turn, covalently linked to a targeting moiety. (T), wherein the compound is represented by a formula X-L1-P-L2-T or pharmaceutically acceptable salts thereof, wherein L1 and L2 represent at least one linking

moiety.

There is no suggesting in the Tomalia et al. reference to modify its teaching to yield the present invention. Therefore, the Tomalia et al. reference would not have motivated one of ordinary skill in the art to reach the claimed invention when it teaches that genetic material can be complexed with a dendrimer only via a non-covalent association (see col. 47, lines 55-62). Following this reference, one of ordinary skill in the art would have lacked motivation to use its teachings alone or in combination with the teachings of the secondary reference to make the composition of the present invention with a reasonable expectation of success. Absent such reasonable motivation, there can be no *prima facie* case of obviousness. See, e.g., MPEP §2143.

The Examiner relies on a secondary reference Meade et al for the use of Gd(III) as a contrast agent for MRI. However, the secondary reference Meade et al. does not remedy the aforementioned deficiency of the primary reference, the Tomalia et al. reference, to teach or suggest all the limitations of the base claim 1 because Meade et al. do not disclose utilizing PNA covalently bound to a dendrimer and or targeting messenger RNA in a cell. Moreover, tt would not be obvious to a person skilled in the art to substitute DNA with PNA and have a reasonable expectation of success because PNA is insoluble in water and aggregates easily.

Thus, the proposed combination of Tomalia et al. and Meade et al. fails to render base claim 1 obvious.

Claims 4, 7-16, 26-28, 34, 41-45, 48, 49, 52, 54-56, 69, 70, 73, 75, 83, 85, 86 and 88 depend from base claim 1 and are unobvious over the Tomalia et al. reference in combination with the Meade et al. reference for at least the same reasons base claim 1 is unobvious.

Accordingly, reconsideration and withdrawal of the Section 103 (a) rejection of claims 1, 4, 7-16, 26-28, 34, 41-45, 48, 49, 52, 54-56, 69, 70, 73, 75, 83, 85, 86 and 88 are respectfully requested.

103 (a) rejection over Lewis et al. taken with Basu et al. in view of Tomalia et al.

Claims 1-4, 28-32, 34, 69, 71-73, 76-81, 83, 85 and 86 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis et al. taken with Basu et al., as applied to claims 1-4, 28-32, 34, 69, 71-73, 76, 80, 81, 83, 85 and 86 above, in view of Tomalia et al. This rejection is respectfully traversed.

As discussed above, Lewis et al. do not describe a "targeting moiety" contemplated in this invention and Tomalia et al. do not teach a compound comprising a dendrimer (X) covalently linked to a PNA (P), which is, in turn, covalently linked to a targeting moiety. (T), wherein the compound is represented by a formula X-L1-P-L2-T or pharmaceutically acceptable salts thereof, wherein L1 and L2 represent at least one linking moiety.

Thus, even if combined, the references would not yield the composition of the invention as described in the amended base claim 1.

Further, the Nakano et al. reference does not cure the deficiency of the combined reference to teach or suggest all the limitations of the base claim 1 because Nakano, et al. teach multiple intratumoral injections of an adenovirus that overexpresses 347 nucleotides of KRAS RNA to lower translation of KRAS mRNA and slow the growth of colorectal cancer xenografts in mice. Further, Nakano, et al. do not teach probe (short oligonucleotide less than 20

nucleotides) binding to specific receptors on cells, probe internalization into cells via receptor, probe release into cellular cytoplasm, or probe binding to mRNA in cellular cytoplasm.

Therefore, base claim 1 is unobvious in light of a combination of all named references.

Claims 3, 4, 28-32, 34, 69, 71-73, 80, 83, 85, 86 and 88 depend from base claim 1 and are unobvious over the Tomalia et al. reference in combination with the Lewis et al. reference or further in combination with the Nakano et al. reference for at least the same reasons base claim 1 is unobvious.

Accordingly, reconsideration and withdrawal of the Section 103 (a) rejection of claims 1, 3, 4, 28-32, 34, 69, 71-73, 80, 83, 85, 86 and 88 are respectfully requested.

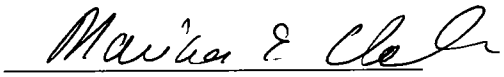
For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.

August 28, 2006

By: 

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